OBSERVATIONS

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DIAGNOSIS OF DIPHTHERIA

AND

A STUDY OF ITS LOCAL TREATMENT.

BY

FRANCIS H. WILLIAMS, M.D.

(Reprinted from the Boston City Hospital Medical and Surgical Reports.)

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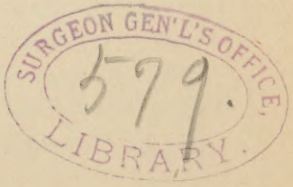

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OBSERVATIONS ON THE DIAGNOSIS OF DIPHTHERIA AND A STUDY OF ITS LOCAL TREATMENT.

By FRANCIS H. WILLIAMS, M.D.

Presented at a meeting of the Suffolk District Medical Society, Boston, April, 1894.

I SHALL assume that diphtheria is caused by the Klebs-Lœffler bacillus and begins as a local disease. The diphtheria bacillus flourishes chiefly in the throat and is not a motile bacillus, but must be carried to the healthy individual. This is done principally by direct transferrence from mouth to mouth, or hand to mouth or nose. By mouth to mouth I mean, for example, a healthy child may catch diphtheria by biting from the same apple, putting the same toys in the mouth, using the same handkerchief as a child in whose throat diphtheria bacilli are present, or by kissing such a child; or a mother may use her own handkerchief for a neighbor's ailing child, and thus unwittingly carry the disease to her own children. The closer contact among children, and the habit they have of putting things in their mouths, shows why the disease is more prevalent among them than among adults. The bacilli may get on to the hands of those who are taking care of or are about persons ill with diphtheria, and unless the hands are carefully washed may be transferred to the mouth at the next meal on a piece of bread, for instance. Again the bacilli may live for months in the garments of a person who has been ill with diphtheria. But I need not multiply examples as to the mode of contagion.

The bacilli, once conveyed to the mouth or nose, may remain in the throat some days, or more than a week even, without showing any sign of their presence, and in some cases may produce no symptoms of disease, although during this

period such individuals may give diphtheria to others; but in the usual course of things the presence of bacilli in the throat is followed, probably within a day or two, by congestion, although this congestion may not be marked, and usually the tonsils, palate, or pharynx are first attacked; this congestion is sometimes accompanied by much œdema and swelling, and is generally soon followed by the appearance of false membrane, which may at first cover a small area only, but following the spread of the congestion may appear in new areas on each day for a few days; in other words, the mucous membrane is, as it were, planted with bacilli, and the false membrane results, but the crops may not all appear at once. Most of the bacilli are found in the outer portions of the false membrane. In a word, the natural history of the disease seems to be: bacilli on a most alkaline surface, at a temperature favorable to their growth, irritation, congestion, false membrane. This membrane may disappear from the throat before the bacilli. Therefore in the beginning and at the close of the disease an individual is especially dangerous to the community, because in the first case his diseased condition is unsuspected or thought of slight consequence, and in the second case because the normal appearance of the throat, although the bacilli may still be present, leads to the belief that the danger of contagion from him is past. The bacterial test, therefore, is of special importance in these two stages of the disease, as it is the only means of detecting the diphtheria bacilli.

In 1892 I began to employ the bacterial test for my patients and initiated its use at the Boston City Hospital. Since the beginning of 1893 this test has been carried out without interruption in the pathological laboratory of the hospital, under the direction of Prof. W. T. Councilman, and it has now been applied to a large number of cases, among them to more than 500 of my patients. A number of bacterial examinations have also been made for my patients in the laboratory of the Harvard Medical School.

As already stated, there are two stages of diphtheria in which this test is especially serviceable.

First. Very early in the disease, before the throat shows any trace of false membrane.

Second. Late in the disease, after the false membrane has disappeared; that is, during convalescence.

Let me illustrate the *first class* of cases by giving the history of a household in which a case of diphtheria occurred. A patient of Dr. James J. Minot, a boy of eight years, had sore throat with membrane on a certain Sunday; bacterial examination showed on Monday evening that the bacilli of diphtheria were present. Dr. Minot then put the patient under my care. The throats of the other members of the household presented no signs of diphtheria, but it seemed to me wise to follow my rule and have swabs taken from the throats of all. They were also taken by Dr. Minot from the throats of those outside of the household who had been much with the patient. In three of the members of the household bacilli of diphtheria were found, although, as already stated, there was nothing to indicate diphtheria to the unaided eye when the swabs were taken for diagnosis. One of these three throats was carefully examined with the mirror by a laryngologist shortly after the swab was taken and he found no sign of diphtheria. Thirty hours later there was no indication of membrane in two of these throats. Treatment with strong hydrogen-dioxide acid solution was begun on all these cases as soon as the Klebs-Lœffler bacilli were found, and in one of the adults the dioxide made conspicuous the false membrane on the right tonsil and anterior pillar which was barely visible just before its application. No membrane was seen at any time in the throat of the second patient, a boy of two years. After three days' treatment with strong hydrogen-dioxide solution the bacilli of diphtheria were not found in cultures from his throat. The third member of the household referred to above, the nursery-maid of the first patient, had no sign of false membrane in her throat twenty-four hours after the swab was taken, but within a day or two it spread to nearly every part of the throat within sight, or which could be seen by depressing the tongue strongly. The diagnosis of diphtheria could not have been made in these cases, except by these bacterial examinations, at the stage of the disease when the swabs were taken. These four cases all recovered.

The advantages of early diagnosis, of early isolation, and

early treatment are seen by contrasting the above-mentioned household with the following family:

In this family, a child was taken ill with diphtheria, a few days later a second child, who died soon after at home, and at short intervals two other children, the mother and aunt. Three children, the mother, and aunt came to the Boston City Hospital and were under my care. The children came too late to be helped, and all died. The mother and aunt were the last members of the family to show signs of the disease; they entered the hospital when they had been ill three and four days respectively, and recovered.

Such experiences show that as soon as a case of diphtheria is found in a household, the bacterial test should be applied to all its members, though their throats may be normal in appearance. This would lessen the spread of the disease and give more patients the great advantage of early treatment; in some cases this might be begun before any other warning had been given than the presence of the bacilli.

In the *second class* of cases — that is, during what I may call convalescence — we frequently find that although the throat of a given patient looks perfectly well, yet it still contains bacilli, and isolation has therefore to be continued. The safeguard which bacterial examinations of the throats during the convalescent stage may be to the community is well illustrated by one of my patients (treated locally with corrosive sublimate 1 to 10,000, and a weak (10 volume) solution of hydrogen dioxide), from whose throat the false membrane had disappeared and who had expressed a hope to be at home for the Thanksgiving festival. Formerly, discharge being determined by the inspection of the throat only, she would have been allowed to leave the hospital much before the desired date. The bacterial test, however, which was made at short intervals for some weeks after the date of the festival referred to above, showed the bacilli to be present. One shudders to think of what might have followed her contact with the children of the family, and how, originating with her, the disease might have spread to other families.

In a former paper[1] I have referred to the persistence of

[1] "American Journal of the Medical Sciences," November, 1893.

the bacilli in the throat for some weeks, and in one patient (treated locally with corrosive sublimate 1 to 10,000) for nearly three months, and pointed out the necessity of making a bacterial examination of the throats of patients before isolation is terminated.

We now come to another stage of the disease in which there are acute appearances in the throat, with false membrane. In these cases the Klebs-Lœffler bacilli are usually found. We may find cases, though they are uncommon, in which one, two, or even three examinations fail to find the bacilli of diphtheria, although direct examination of the membrane itself sometimes shows them to be present. Further, we may have cases in which no bacilli are found in the first examination, but subsequent trials show them to be present; and, finally, we may have cases in which the bacterial examination during life fails to find them, although a post-mortem examination reveals them. On the other hand, unless the test is carefully made it is quite possible to mistake some other bacillus for the bacillus of diphtheria. I therefore feel called upon to repeat my statement of last year, that these examinations are not infallible; but when all precautions have been carefully taken, and more than one examination made, I believe that they may usually be relied upon, except in cases where the disease is laryngeal, and that we are certainly justified in taking a much more favorable view of the recovery of a patient in whose throat the bacilli are not found than in those where they are found, although the appearances in the throat may be similar in both. Failure to find the Klebs-Lœffler bacilli may mean that they have perhaps become less abundant through the more vigorous growth of other and less dangerous organisms. It may be that this is one of nature's ways of limiting diphtheria. The diphtheria cases which give a pure or nearly pure culture of the bacillus seem to be very fatal[1] unless efficient treatment is employed, so far as one may infer from 47 cases in which the mortality was 64%. A local treatment, which I shall describe later, is, I think, especially effi-

[1] It is important to realize that if the pulse in diphtheria suddenly changes during the acute stage of the disease and takes on the character indicative of a low blood-pressure, the prognosis is very grave, no matter how well the patient may appear to be in all other ways.

cient in cases where the Klebs-Lœffler bacillus only is found; nine cases giving a pure or almost pure culture of the diphtheria bacillus in which this treatment was used early all recovered.

As regards cases with false membrane in which the diphtheria bacilli are not found. In 50 cases of what may be called pseudo-diphtheria, occurring in different years, there was a mortality of 28%. As these cases were designated as pseudo-diphtheria on account of the absence from the bacterial test of the Klebs-Lœffler bacillus, we shall do well to look into this high mortality of 28%, or 14 out of 50 cases, a little more closely. These 14 cases, in about an equal number of instances, contained either streptococci or staphylococci, or both together.

10 were laryngeal, with 7 intubations,
1 had typhoid fever,
1 scarlet fever,
1 septic, with nasal discharge,
1 had nasal discharge.

14

Both the cases with nasal discharge were two years old, and in wretched condition when they entered the hospital.

Excluding the case of typhoid fever, there are two features which most of these 14 cases had in common; that is, their laryngeal character and their extreme youth — the average age was three years. It seems to me that these conditions determined the fatal outcome in these cases rather than any special coccus, or, what is more probable if we take the ground that the laryngeal cases are usually diphtheria, the Klebs-Lœffler bacilli probably escaped detection in some of them. As autopsies were not obtained, this point could not be determined.

In studying diphtheria one is struck by the large number of cases in which the larynx is involved and the high mortality among such cases. As we continue to use the bacterial test and obtain more autopsies I think we shall find that the percentage of fatal cases of membranous throats where the bacillus of diphtheria is absent will be smaller. Large numbers of cases of so-called pseudo-diphtheria already reported

by other observers, in which the mortality is very low, point to this conclusion. If the bacterial test has been carefully made, no bacilli of diphtheria found, and the larynx and nose are not involved, the prognosis of cases of membranous throats, where no other disease is present, — such as typhoid fever, pneumonia, measles, or scarlet fever, — is usually good. Of such cases my experience thus far has justified me in taking a hopeful view. I recall a case seen in consultation where the physician in charge had given a wholly hopeless prognosis, but the bacterial examination and the general condition of the patient led me to take an opposite view, which proved to be the correct one.

The inferences which may be drawn from suspicious cases seem to be these: First, cases which come to the hospital looking like diphtheria usually are such; that is, perhaps about nine times out of ten. The milder cases of membranous throats are not sent to the hospital in such large numbers as the severer ones, and thus the proportion of cases of diphtheria is smaller in suspicious cases if seen outside of the hospital; this has been my experience in private practice. Second, cases which look like tonsillitis, for example, usually are such, although now and then among such cases the bacilli of diphtheria are found. In practice it is well at first to regard everything which resembles diphtheria as diphtheria, until careful bacterial tests have been made.

Before leaving the subject of diagnosis, allow me to remind you again of the importance of recognizing the mixed cases of diphtheria and scarlet fever; these are doubly dangerous, as they may give rise to either disease in other individuals, especially in a hospital for contagious diseases, and require special and careful isolation. In 1892, when I first saw these mixed cases, that is, found the Klebs-Lœffler bacillus *coincidently* with scarlet fever in certain patients, their presence was denied by most of those, at least in this country, who had given the question special study, but now their existence has, I think, been generally recognized.[1]

[1] In scarlet fever it seems to me desirable to prevent the dissemination of the epithelial scales, which are often shed abundantly, and to hasten the removal of this layer of epithelium in order to free the normal skin. For this purpose I have my patients rubbed all over, daily, avoiding the hair, with a mixture containing seven parts of a 10-volume solution of hydrogen dioxide with one part of glycerine; if the

Three cases of typhoid fever with membranous throats in which bacilli of diphtheria were found, occurred during my service; one of these has already been referred to in a former paper of mine ("American Journal of the Medical Sciences," November, 1893), and Dr. John L. Morse has described a second of these cases (Isabella N.) in the Boston City Hospital Report for 1894. In my above-mentioned paper I also referred to the coincidence of diphtheria and measles during my service.

It is not very rare to see patients with syphilis presenting appearances in the throat similar to those found in diphtheria (of course both diseases may occur together); if syphilitic patches occur with an acute tonsillitis or pharyngitis the similarity to diphtheria is more striking.

Let us now consider the local treatment of diphtheria, first from the laboratory, and, second, from the clinical side.

The micro-organisms, dangerous above all others in the throat, are the venomous bacilli of diphtheria, and an early attack upon them with a suitable application diminishes the amount of the poison and probably prevents the extension of the bacilli to less accessible parts.

A rational step to be taken in our endeavor to destroy the bacilli is to ascertain what germicides will find and kill them quickly, and also which of the germicides, sometimes used, will not do so. I say find and kill, as there are many applications which will kill the bacilli in the laboratory, but when used in the throat simply wash the surface of the false membrane; there is one, however, which is an exception to this, as it has the quality of promptly disintegrating certain portions of the false membrane. In the plan which I adopted in the study of the action of various germicides upon the Klebs-Lœffler bacillus and several of the organisms which sometimes accompany it, I assumed that the germicide to be efficient must act quickly, as the contact in the throat between the germicide and the organisms is limited to a few seconds. It was, therefore, necessary to ascertain what would kill these organisms in five or ten seconds.

patient finds this too sticky the proportion of glycerine may be reduced. A quarter of the body may be done at one time, and some hours later another quarter, and so on. As soon as any portion of the skin is normal the application may be there dispensed with.

Second, if an agent or agents could be found to kill the organisms in five or ten seconds, the next step would be to ascertain what harmful effect, if any, they could have upon man, and to select one or more of those which would be least injurious to him: many germicides, such as corrosive sublimate, carbolic acid, the cresols, hydrochloric, nitric, phosphoric, and sulphuric acids alone and in efficient strengths are either poisonous or irritating, or both.

The third step in the investigation would be to learn how to apply efficiently a substance quickly fatal to the organisms and harmless to man, provided such a substance could be found.

Tests with various germicides were made under my direction, or by me, in the Biological Laboratory of the Massachusetts Institute of Technology upon the bacillus of diphtheria, the staphylococcus pyogenes aureus and albus, the streptococcus pyogenes, and a diplococcus, and I wish to express here my appreciation of Prof. W. T. Sedgwick's kindness in permitting me to use his laboratory, and my obligations to his former and present assistants, Messrs. McLauthlin, Mathews, and Keith, for carrying out many of these tests.[1]

[1] The following outline taken from a former article will show the method pursued. In any of the ordinary methods for the determination of the germicidal action of any liquid disinfectant upon a given bacterial species, three distinct and successive processes may usually be recognized. These are: first, the mingling for a known period of a pure culture of the given species with a suitable amount of the germicide; second, the dilution, after the desired interval has elapsed, of this mixture to the extent necessary not only to check further bactericidal action, but also to avoid the possibility of any future inhibitory effect; and third, the planting of a portion of this dilution in a suitable culture medium, in order to permit the growth and consequent recognition of any bacteria which may have survived the action of the germicide.

As a source of the diphtheria bacillus, we used a pure culture that came originally from the laboratory of Dr. Welch, of Johns Hopkins University, or one from Dr. Prudden's laboratory in New York, or from my own cases. From these, plantings were made in bouillon, and to ensure greater accuracy, in most of the experiments old and fresh bouillon cultures were used side by side, or a mixture of the two was employed.

The following record of a single action experiment with its control will serve to illustrate this method.

Five c.c. of 50-volume dioxide solution (⅛% acid) were placed in a 60 c.c. Erlenmeyer flask and 0.25 c.c. added of a bouillon culture of the diphtheria bacillus. (In later tests, the germicide was poured over the culture.) Ten seconds after, in order to stop the action of the dioxide, the mixture was quickly poured into a litre flask containing 600 c.c. of slightly alkaline normal salt solution. Thirty seconds after this, the whole having been well shaken, 0.2 c.c. were transferred to 75 c.c. of alkaline normal salt solution in another flask. At the end of three minutes (in the

All of the tests given in the following tables, besides many others, have been made in duplicate, and some have been repeated several times.

TABLE I. — Tests with various Germicides upon the Klebs-Lœffler Bacillus.

Action period, 10 seconds.

Germicide.	Did not kill all.	Killed all.
[1] Hydrochloric acid	3%	4%
[1] Nitric acid		2%
[1] Sulphuric acid	5%	10%
[1] Phosphoric acid	2%	
Boric acid	4%	
Solution of chlorinated soda (hypochlorite of sodium), containing of available chlorine	1–2500	1–1000
[2] Chlorine	1–25000	1–10000
Corrosive sublimate	1–10,000 (0.01%)	1–5000 (0.02%)
Chloroform (in water)	1–200	
Carbolic acid	[4] 5%	[4] 5%
Tricresol in 25% alcohol		3%
[3] Metacresol in water		½%
Paracresol in water		½%

later experiments at the end of thirty seconds), 1 c.c. of the last dilution was planted in 6 c.c. of the bouillon. At the end of four and a half minutes 1 c.c. of the dilution was added to 6 c.c. of melted glycerine agar at 40° C., and the mixture at once poured into a Petri dish.

In the control experiment, 0.25 c.c. of the bouillon culture of the bacillus were mixed with 600 c.c. of alkaline normal salt solution, *then* 5 c.c. of 50-volume dioxide (⅙ % acid) added, and all were shaken. Thirty seconds after the addition of the dioxide, 0.2 c.c. of the mixture were transferred to 75 c.c. of alkaline normal salt solution in another flask. After four and a half minutes, a glycerine-agar plate was made as before.

After a few days' growth in the incubator, the agar plate from the control experiment showed 1,600 colonies of the diphtheria bacillus. At the same time, neither the agar plate, nor the bouillon tube, prepared from the action experiment, showed any growth.

Evidently the agar plate is of especial advantage when a part only of the bacteria are killed, *i.e.*, when the germicide is diluted just beyond its effective limit. The bouillon tube gives no precise means of distinguishing between the survival of a part and the survival of the whole of the bacteria.

[1] U.S. Pharmacopœia dilute acid contains 10 per cent. of acid.

[2] Chlorine water contains 0.4 per cent. of chlorine, which diluted with 99 parts of water, gives 1–25000. Chlorine water cannot be mixed with hydrogen-dioxide solutions.

[3] I have used a solution containing ½ % of metacresol and 25-volume acid hydrogen-dioxide in twenty-five cases of diphtheria; objection has been made to the taste by some patients, and it seems to me to be less satisfactory than a strong hydrogen-dioxide solution alone.

[4] Does not always kill.

TABLE II. — Tests with various Germicides upon the Staphylococcus Pyogenes Aureus.

Action period, 10 seconds.

Germicide.	Did not kill all.	Killed all.
Hydrochloric acid	2%	4%
Nitric acid	½%	2%
Solution of chlorinated soda (hypochlorite of sodium), containing of available chlorine	1–2500	1–1000
Corrosive sublimate	1–5000	
Carbolic acid	1%	2½%
Tricresol in water	1%	1%
Metacresol in water	¼%	½%
Paracresol in water	½%	½%
Orthocresol in water	½%	

Staphylococcus Pyogenes Albus.

Germicide.	Did not kill all.	Killed all.
Hydrochloric acid	2%	4%

TABLE III. — Tests with various Germicides upon the Streptococcus Pyogenes.

Action period, 10 seconds.

Germicide.	Did not kill all.	Killed all.
Hydrochloric acid	⅛%	½%
Nitric acid		½%
Solution of chlorinated soda (hypochlorite of sodium), containing of available chlorine	1–2500	1–1000
Corrosive sublimate	1–10,000	1–5000
Carbolic acid	1%	5%
Metacresol in water	¼%	½%
Paracresol in water	¼%	

From these tables it will be seen that with the exception perhaps of the solution of chlorinated soda (hypochlorite of sodium) and the cresols, there is no one germicide that is equally active against all of these organisms. In general it may be said that the streptococcus pyogenes is the easiest to kill, the staphylococcus aureus the most difficult. A few tests

made upon the staphylococcus pyogenes albus indicate that in this respect it is similar to the aureus. A weak solution of hydrochloric acid, ½%, will kill the streptococcus in ten seconds, but it takes a 4% solution to kill the Klebs-Lœffler bacillus in the same time. It takes about the same strength to kill the staphylococcus aureus and albus. The staphylococcus aureus is more resistent to corrosive sublimate than these other organisms; on the other hand, it is more susceptible to carbolic acid than they are.

It should be remembered that in the laboratory tests the micro-organisms are presented to the germicides in a liquid culture, whereas clinically they are found enveloped in a mass of pus or false membrane, or other matter. Hence the advantage of using the substance I am about to consider.

To discuss the action of all the germicides I have studied during my work on diphtheria would not be feasible here, but I will devote a few words to one of them: namely, hydrogen dioxide.

The general principle in antiseptics which my studies have brought out, and which I believe to be a new one, is the advantage of mixing the stronger germicides with hydrogen dioxide, a substance which has the special property of disintegrating some kinds of dead organic matter, such as pus, or certain portions of false membranes, thus rendering the bacilli more accessible, and so opening the way for the action of the stronger germicides. Pure hydrogen-dioxide solutions, or rather neutral solutions, are comparatively weak germicides, but we may put with them any compatible germicides, or use them alternately with an incompatible one, the choice depending upon the micro-organisms we desire to kill. For instance, the mineral acids which are found in all the 10-volume hydrogen-dioxide solutions sold in the market increase the germicidal value of these solutions. A 20-volume or even a 40-volume neutral solution of hydrogen dioxide will not kill all the streptococci in 10 seconds, but a weak solution of hydrochloric or nitric acid will do so. Tests, therefore, of the germicidal value of the hydrogen-dioxide solutions should always take into account the kinds and amount of free acid present.

TABLE IV. — TESTS WITH HYDROGEN–DIOXIDE NEUTRAL AND ACID SOLUTIONS UPON THE KLEBS–LŒFFLER BACILLUS.

Action period, 10 *minutes*.

Did not kill all.

$2\frac{1}{2}$ volumes containing . . . . . 0.05% of acid.[1]

This is stronger in acid than a U.S. Pharmacopœia 10-volume hydrogen-dioxide solution diluted with three parts of water, a strength which is frequently used by physicians.

Action period, 10 seconds. Did not kill all.			Action period, 5 seconds. Killed all.		
5	volumes containing	0.1% acid.	50 volumes containing		0.17% acid.
[2] 10	" "	0.2% "	100 "	" about	0.3% "
$12\frac{1}{2}$	" "	0.25% "	150 "	" "	0.45% "
[3] 25	" "	0.5% "	200 "	" "	0.6% "
50	neutral or slightly alkaline.		250 "	" "	0.9% "

TABLE V.— TESTS WITH HYDROGEN–DIOXIDE NEUTRAL AND ACID SOLUTIONS UPON THE STAPHYLOCOCCUS PYOGENES AUREUS.

Action period, 10 seconds. Did not kill all.			Action period, 5 seconds. Killed all.		
25	volumes containing	0.5% acid.	100 volumes containing		1% acid.
50 "	"	1.1% "	110 "	neutral.	
80 "	"	0.26% "			

Staphylococcus pyogenes albus was also killed by a 100-volume hydrogen-dioxide solution containing 1% acid.

TABLE VI. — TESTS WITH HYDROGEN–DIOXIDE NEUTRAL AND ACID SOLUTIONS UPON THE STREPTOCOCCUS PYOGENES.

Action period, 10 seconds.

Did not kill all.			Killed all.		
10	volumes containing	0.05% acid.	25 volumes containing		1.1% acid.[4]
10 "	"	0.10% "	$12\frac{1}{2}$ "	"	0.5% " [4]
20 "	neutral or slightly alkaline.				
40 "	" "	" "			

[1] The acid was estimated as HCl with a 1-100 normal NaOH solution and phenolphthalein.

[2] The U.S. Pharmacopœia 10-volume solution contains not more than 0.036% of acid.

[3] Sometimes a 25-volume solution containing 1-6 per cent. acid will kill, and sometimes it will not kill.

[4] The tests given in Table III., made later than these, show that 0.5 per cent. of hydrochloric acid alone " killed all " in ten seconds.

Tests with hydrogen-dioxide acid solutions upon a diplococcus from the throat of a patient ill with diphtheria showed that a 25-volume solution containing 0.1% acid did not kill in ten seconds, but that a 50-volume solution containing 0.1% of acid did kill in ten seconds.

It is not assumed that these bacterial tests have the accuracy of chemical ones. I have found nothing, however, which vitiates the general character of the deductions drawn from these tests: First, that neutral hydrogen-dioxide solutions are comparatively weak germicides: second, that the mineral acids, especially nitric acid, are stronger germicides; third, that hydrogen dioxide and hydrochloric acid together are more efficient than either alone against the Klebs-Lœffler bacillus; and fourth, that the 50-volume (0.2% acid) hydrogen-dioxide solution is not a good germicide against the staphylococcus, — 100-volume hydrogen dioxide acid (1%) solutions are required to kill this organism in five seconds. I hope to discuss the more general applications of these tests in another paper.

I observed an interesting correspondence between the laboratory tests and clinical experience in several cases, and will recur to this point.

We now come to the clinical side of the local treatment of diphtheria, and the treatment to which I wish to direct your attention is that with strong hydrogen-dioxide acid solutions.[1] The mortality in this State from diphtheria is greatest during October, November, December, and January, and my last service at the Boston City Hospital included the three latter months, November and December, 1893, and January, 1894, but I have permission to consider here the cases that were admitted in October, 1893, also.

On the mild, as well as on the hopeless cases, a 10-volume solution of hydrogen dioxide was generally used, alone or in connection with a solution of corrosive sublimate (1–5000 or 1–2500) or a solution of chlorinated soda. On *all* of the severer cases which came in the early days of the disease,

[1] I have found these strong solutions useful in minor surgery; they should not be used in closed cavities, as too much oxygen might be set free and cause pressure.

As a dressing for sores or ulcers, one may use a 10-volume solution of hydrogen dioxide containing 0.1—0.2 per cent. of hydrochloric acid; when desirable, pepsin may be added to this solution. The dioxide does not interfere with the action of the pepsin.

and during my service, I endeavored to use a 50-volume hydrogen-dioxide acid solution at short intervals.

To illustrate the advantages of using the 50-volume solution, let me take four patients who entered the hospital about the same time:

Two cases of diphtheria treated with a 10-volume solution of hydrogen dioxide.

P. H., 21 years old, entered the hospital December 1st. Klebs-Lœffler bacilli found in the cultures. Thick false membrane on both tonsils and on the sides of the pharynx. Under treatment of 10-volume hydrogen-dioxide solution every four hours the membrane had disappeared on December 20th, but there were still bacilli of diphtheria present on December 20th and 23d. The membrane returned again on January 1st. On January 3d no bacilli were found.

H. N., 6 years old, entered the hospital on December 2d. Klebs-Lœffler bacilli found in the cultures. Small specks of false membrane on right tonsil and right palate. Ten-volume solution every three hours. Bacilli still present on December 25th; absent January 5th.

Two cases of diphtheria: the first one treated in part and the other wholly with a 50-volume solution of hydrogen dioxide.

S. M., 10 years old, entered the hospital on December 3d. Bacilli of diphtheria found in the cultures. This case seemed more severe than either of those above mentioned. False membrane on both tonsils, left palate, right anterior pillar, right and left wall of pharynx. At first a 10-volume solution was used, but as the membrane increased a 50-volume solution was substituted. Bacilli of diphtheria present December 10th; absent December 16th.

J. W., 6 years old, entered the hospital December 8th. Bacilli of diphtheria found in cultures. A more severe case than any of the above. Thick false membrane on both tonsils, and on both anterior pillars. The next day it covered the right, left, and posterior pharyngeal wall. The use of fifty-volume hydrogen-dioxide acid solution was then begun. Bacilli of diphtheria were present on December 11th, throat clear on December 16th, bacilli absent December 17th.

Of these four cases the last two to enter the hospital pre-

sented more severe local symptoms than the first two, the last one especially. The patients who entered the hospital December 1st and 2d, respectively, had a 10-volume hydrogen-dioxide solution applied, and the bacilli were absent January 3d and 5th respectively. Average duration of bacilli, 34 days. The patients who entered the hospital December 3d and 8th, respectively, had 50-volume hydrogen-dioxide acid solution and the bacilli were absent December 16th and 17th respectively. Average duration of bacilli 11 days.

The three following cases further illustrate this point. The patients were adults of about the same age.

Case No. I. — Membrane on tonsils and posterior pharynx. Cultures were made from the throat about every four days and bacilli of diphtheria found. On the 53d[1] day of the disease bacilli of diphtheria still found in the cultures; on the 56th day none were found. The treatment in this case was 10-volume hydrogen-dioxide solution every hour, corrosive sublimate 1–2500 on a swab every two hours. Finally some of the strong hydrogen-dioxide solution was used; after this had been applied for about three days the bacilli disappeared.

One case of diphtheria in which a *partial* use of the strong dioxide acid solutions was made.

Case No. II. entered the hospital more than two weeks later than No. I. Membrane on both tonsils. Klebs-Lœffler bacilli found in the cultures. As there was no strong dioxide solution at hand a 10-volume dioxide solution was used every two hours, followed by 1–2000 corrosive sublimate with 1% citric acid on swab. During the treatment the membrane spread and covered besides both tonsils, the soft palate on both sides, anterior and posterior pillars, and the left and posterior wall of the pharynx. As soon as the strong dioxide arrived, the above treatment was stopped and a 50-volume hydrogen-dioxide solution was applied every two hours by day and every three hours by night for three days; then the intervals between the treatments were in-

[1] The duration of the bacilli in this case is above the average duration of the bacilli in the 23 cases alluded to later, in which the treatment was a 10-volume solution of hydrogen dioxide alone, or in connection with corrosive sublimate or chlorinated soda; but in two other of these cases the bacilli were present in the cultures three weeks longer than in this case.

creased. After the culture made for diagnosis, no subsequent culture, unfortunately, was made until the 26th day of the disease. No bacilli were then found or afterwards. This patient was discharged from the hospital two weeks earlier than No. I., and entered, as above stated, more than two weeks later.

One case of diphtheria, in which a *complete* use of the strong hydrogen-dioxide acid solutions was made.

Case No. III. — This case entered the hospital a month after No. I. Klebs-Lœffler bacilli found in the cultures. The membrane was everywhere on tonsils, palate, uvula, pharynx, both sides and back, and in nose, — a case which justified the old-fashioned term of putrid sore throat. A 50-volume hydrogen-dioxide solution was applied in spray every three hours during the day and twice during the night for five days; a 25-volume solution was then substituted, which was applied three times during the day. No bacilli were present in a culture made on the 8th day of the disease nor at any subsequent examination. The throat of No. III. was free from bacilli two weeks earlier than No. I., although the patient entered the hospital a month later than No. I.

An estimate of the advantage in using the 50-volume solution, in point of the duration of the bacilli, is shown better by comparing the average time during which the bacilli remained in the throats of the milder cases which were treated with a 10-volume solution of hydrogen dioxide alone, or in connection with a solution of chlorinated soda or corrosive sublimate, with the average time during which the bacilli remained in the throats of patients, more severely ill, but who on the other hand were treated with 50-volume hydrogen-dioxide solutions. Most of both sets of cases occurred during about the same months.

In the first class of cases, 23 in number, the bacilli were found on the average to be present in the cultures on the 27th day of the disease and absent on the 36th day of the disease. No cultures were made between the two periods from which these averages were made up. The average age of these cases was 17 years.[1] In the second set of cases

[1] Since the above was written I have used 0.5 per cent. salt solutions in 11 cases. In these the bacilli were found to be present on the average on the 26.3 day of the dis-

(severer ones), namely, those treated with strong hydrogen-dioxide acid solutions, 26 in number,[1] the bacilli were found on the average to be present in the cultures on the 12th day of the disease and absent on the 18.8 day of the disease. No cultures were made between the two periods from which these averages were made up. The average age of these cases was 19.4 years.

It is hardly necessary to point out that the strong dioxide would probably have driven the bacilli from the throats of the milder cases sooner than it did from the severer ones.

In two-thirds of the 26[1] cases treated with strong hydrogen-dioxide acid solutions, the *bacilli* disappeared *before* the *membrane;* in the remaining third this point was not determined. The patients were not discharged from the hospital until both bacilli and membrane had disappeared.

The capacity of a hospital for the treatment of diphtheria would be increased by using the local treatment with strong hydrogen-dioxide solutions rather than those ordinarily employed, as the patients would remain in a diphtheria ward a shorter time.

The *diminution* of the bacilli in the throat under different treatments may be studied by examining a cover-glass preparation under the microscope made from swabs taken directly from the throat. This was done in a few cases only. After a patient had had, for example, a **10**-volume hydrogen-dioxide solution for ten days, bacilli of diphtheria and other organisms were readily found. In cases treated with **50**-volume hydrogen-dioxide solution examined in the same way from two to seven days after beginning treatment, very few organisms of any kind were found; bacilli were, however, found in cultures in these cases for a longer period than in the cover-slips; these examinations show the marked and rapid diminution in the number of bacilli under the treatment by a 50-volume hydrogen-dioxide solution.

case and absent on the average on the 35.4 day of the disease. No cultures were made between the two periods from which these averages were made up. One of these 11 cases had what may be described as a raw-beef throat — a condition which lasted nearly as long as the bacilli remained in the throat, which was six weeks.

[1] These cases are 26 of the 30 cases taken up on page 31; of the four remaining cases, two died and two had no bacterial test applied before discharge; therefore they could not be taken into consideration here.

The following case is one of those which illustrates how the 50-volume hydrogen-dioxide acid solution may kill the diphtheria bacilli in a wound:

A patient ill with diphtheria had a contused wound, which was incised and the pus let out. A swab was taken from the wound and the culture made from it was an almost pure culture of diphtheria bacilli. The flaps of thick dead skin were trimmed off, leaving an open wound about an inch in diameter, covered with pus. The wound was cleansed with 50-volume hydrogen-dioxide acid solution on a mop and covered with gauze moistened with a 10-volume solution. Four hours later the gauze was removed and a second swab taken; no diphtheria bacilli were found, only staphylococci. That the diphtheria bacilli were killed by the 50-volume hydrogen-dioxide solution and the staphylococci were not, is in accord with the laboratory tests.

Since this paper was read, by the kindness of Dr. H. W. Cushing I have used in certain cases in his service (surgical) the strong hydrogen-dioxide solutions—usually 25, sometimes 50 volumes — freely upon large granulating surfaces of burns and ulcers; when they were so situated that the strong dioxide solution could be poured into a cuplike depression of the granulating surface, this was done, and the dioxide allowed to remain some minutes; it was then washed out and more strong dioxide solution poured in; this was repeated several times. The granulating surfaces were cleansed in this way daily for weeks without causing the patient any discomfort, and were dressed with a dilute solution of hydrochloric acid $\frac{1}{10}$ or $\frac{1}{5}$ %. All healed well.

Let us now consider the METHOD of applying the strong hydrogen-dioxide solutions.[1]

The Strength of the Applications. — This should ordinarily be from 25 to 50 volumes, according to circumstances,

[1] How not to use the solutions of hydrogen dioxide in diphtheria is very well illustrated, I think, by some cases that were brought to my attention since this paper was read. A solution of hydrogen dioxide in ether, known as pyrozone, was used to make the hydrogen-dioxide solution. The manufacturers claim that these solutions are nearly neutral; in other words, an important germicidal element, the acid, is left out; the special property of the hydrogen dioxide itself being the disintegrating power. Second, the air-pressure used in the atomizers was too great. The air was pumped up to a pressure of 80 pounds, then allowed to run down to 30 pounds and again pumped up to 80 pounds. The pressure should not be more than 6 or 8 pounds.

containing about $\frac{1}{10}$ to $\frac{1}{5}\%$ of acid. A stronger solution must be used in the throat than in the laboratory on account of the dilution by the saliva. If there is much membrane, and especially if the case is septic and in the early days of the disease, the full 50-volume strength is needed. It is well to make the application with a mop so far as may be, and the spray should be used gently. One should not omit to treat the nose and keep it clear, but a separate atomizer should be used for this purpose. In spraying the nose, only very weak solutions **1** or **2** to **5** volumes should be used. The spray should be directed horizontally into the nostril and not upwards. In the posterior nares the strong solutions may be employed by means of an up-spray, or by a spray directed forwards from the posterior nares; the formation of much foam after the application of the solution to the latter parts indicates the presence of membrane. It is very important to know the acidity and strength of the solutions of hydrogen-dioxide, and the value of the treatment cannot be properly estimated unless analyses of the solutions are made. The different makes vary in the amount of acid and hydrogen dioxide they contain. The 10-volume solutions purchased for the hospital, from which the strong solutions were made, have been excellent. The most efficient mode of application is by means of a gentle spray under an air-pressure of 6 to 8 pounds, just sufficient to carry the solution to the desired spot; this avoids dilution better than when the applications are made on a mop, although sometimes a mop answers well, and it is easier for the patient.

The discomfort of all local applications is usually greatest during the early days of the disease, when the throat is most sensitive and most congested, but at this time treatment is most serviceable. Later in the disease when the false membrane is clearing off, and if a sensitive, raw, congested surface is exposed, especial care should be taken to avoid these sensitive areas or use the dioxide solution on a mop. One should be careful not to cause bleeding. The applications, especially in spray, should be made most gently. If the mop is used, the solution causes much less, sometimes no discomfort. The amount

That the 50-volume hydrogen dioxide solutions are harmless when properly even if very frequently applied, is illustrated by the following case, although before outlining it I should say that I do not consider it justifiable to use any local treatment hourly through the night.

B. R., a girl 15 years old, nursery maid in a family where two children had just died of diphtheria, was sent to the hospital, probably about the first day of the disease, the family being on the alert for any symptoms of diphtheria. Clinically, the appearances in her throat were those of diphtheria, the false membrane covering nearly the whole surface of both tonsils. Unfortunately, no culture was made from the throat when the patient entered the hospital, and the swab taken next morning, after the strong dioxide solution had been applied a number of times, gave no bacilli of diphtheria, only staphylococci and streptococci; and that taken four days later, only staphylococci. There was a trace of albumen in the urine. A new house officer began his service on the afternoon of this patient's arrival, and, through a misunderstanding, the 50-volume dioxide solution was applied every hour through the night, and until my visit in the morning (making about eighteen successive hourly applications) when I reduced the frequency of the applications to once in three hours by day, and directed that she should be waked once at night for an application. The patient made not the slightest objection to the frequent treatment, and, so far as I could see, only good had resulted from it. The congestion was lessened, and the false membrane covered very much less than its original area, and by afternoon — twenty-four hours after entrance — was nearly gone; traces of it were then seen for the last time.

of discomfort is, in most instances, an indication of the want of skill in making the applications. While the smart of the strong dioxide is usually greater at the time than that of some of the other applications which are made to the throat, it is only momentary; patients invariably prefer the strong hydrogen-dioxide solutions to chlorinated-soda solutions of efficient strength. I recall some patients who spoke of the pain the strong dioxide solution caused, and I therefore tried, without their knowledge, spraying their throats with water, and often they did not distinguish between the two. It is the friction of the spray which I think chiefly causes the discomfort, and some throats are evidently more sensitive than others, and some patients more nervous. The majority of patients do not mind the strong dioxide solutions, but many ask to have them applied oftener on account of the relief which follows their use. In an adult where the nose was closed with false membrane and the tonsils so much swollen and covered with false membrane as to cause cyanosis, the throat was cleared in a few moments by the use of strong hydrogen-dioxide solutions, and the breathing was thus made perfectly easy, although a few moments before tracheotomy had been considered.

The Number of Applications.— The strong hydrogen-dioxide solutions should be applied often during the first few days; by often I mean once every two hours by day, and twice during the night for the first night or two in severe cases. It will be found, after a few days, in some cases after two or three, that the diphtheria bacilli are much diminished in number or have even disappeared from the throat, although much false membrane may remain. Their disappearance can only be determined by cultures; false membrane in the throat is not a proof of the presence of the bacilli of diphtheria; it may be due to other organisms. No matter how much membrane there may be in the throat, we may be much relieved when the bacilli have disappeared from the cultures. When this has taken place local treatment should be omitted, except to give comfort to the patient by clearing the throat.

I am inclined to think that the persistence of the Klebs-Lœffler bacilli for more than a week or ten days, under the

strong hydrogen-dioxide treatment, is due usually to their being concealed in the folds of mucous membrane or in pockets which have been made by the inflammatory process, especially in the tonsils, and that the attention should be directed to the application of the solution to these hiding-places carefully and thoroughly.

I observed that in some cases of diphtheria the false membrane persisted under the use of the 50-volume hydrogen-dioxide acid solution for some time after the Klebs-Loeffler bacilli had ceased to be present in the cultures: staphylococci were, however, present. This led me to study the action of the 50-volume solution upon the staphylococcus and to find that it would not kill this organism readily in the beaker. It will be seen in Table V. that a 100-volume hydrogen-dioxide acid (1%) solution is required to kill the staphylococcus in five seconds. Further, I found that chlorinated soda would kill it in the beaker quickly (10 seconds), and that clinically the false membrane that had persisted under the use of a 50-volume solution yielded under the alternate use of the 50-volume solution and a solution of chlorinated soda containing from 1–1000 to 1–500 available chlorine. I have tried this in a few cases only.

The local treatment of membranous throats may, therefore, be best carried on with the microscope and culture tube in one hand and the remedies in the other. As soon as the bacilli of diphtheria have disappeared the strong dioxide should be omitted, except as a cleansing, deodorizing,[1] or disintegrating agent. If we find that the organisms present are chiefly staphylococci we may substitute chlorinated soda for the strong dioxide, or use them alternately, — they should never be mixed nor used too near together, — or we may use hydrogen dioxide and carbolic acid mixed together. The 50-volume dioxide does not kill the staphylococcus readily in the beaker; it will not, therefore, in the throat.

It follows from what has been just said that in treating

[1] A 5 per cent. solution of permanganate of potassium is frequently used as a deodorizer; a saturated solution contains about 6 per cent. of this substance; this would correspond as a source of oxygen to about a 6-volume solution of hydrogen dioxide.

pseudo-diphtheria where staphylococci are present we may use hydrogen-dioxide solution as a disintegrating agent, and chlorinated soda, or carbolic acid, as germicides.

In passing let me add a word of caution as to the use of alkalies in diphtheria. Many practitioners prescribe lime-water in diphtheria, and many are in the habit of prescribing some simple local application containing bicarbonate of soda, such as Dobell's solution, in a case of sore throat. Such alkalies seem to me disadvantageous in diphtheria, as they favor the growth of the bacilli and the formation of their poison; we should, therefore, be careful to avoid them in this disease or where there is a suspicion of the disease. It seems better to have the diseased parts bathed in acid, not alkaline, solutions.

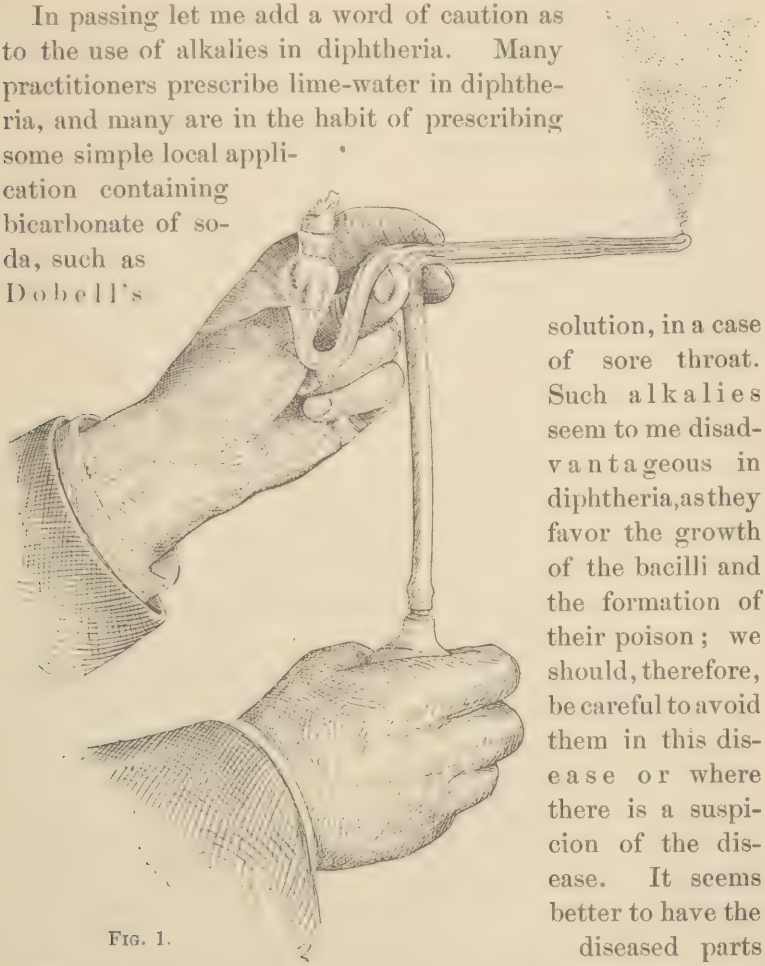

Fig. 1.

From the thumb to the point the tube is 5 inches long. The up-spray is shown in this figure. The top-shaped bulb should not be filled more than one-half full. The mouth of the bulb may be loosely closed with a small roll of gauze (not absorbent cotton) to prevent spattering.

The instruments which I have designed and found efficient for applying the hydrogen-dioxide solutions are, first, three glass atomizers which can be readily sterilized by boiling. One of these has a down-spray, the second a

return-spray, and the third an up-spray. The latter (see Fig. 1) may be used to direct the spray to the side and upper portion of the pharynx or to either tonsil without taking it out of the mouth, simply by turning it in the hand. A spray is best applied to the surface of the tonsils if directed at right angles to it. This can easily be done with this atomizer, which I find indispensable. The rubber bulbs of these atomizers have two valves. I also use an atomizer with a straight spray.

The atomizer for spraying the posterior nares from behind forwards (return-spray) is made by bending the atomizer, shown in Fig. 1, through ninety degrees one-half an inch from its tip.

The mop which I use for swabbing the throat consists of a small glass rod on which some absorbent cotton has been twisted. The rod is about eight inches long and one-eighth of an inch in diameter, and is bent at an angle of about 45 degrees half an inch from the end, in order that the sides of the pharnyx may be more easily reached. The end of the rod is rounded and thickened a little by heating in a flame, as by this device the cotton is held more firmly.

To make the applications with success we should not only have good instruments, but also the coöperation of the patient; it is a mistake to use force — I do not mean that young children should not be held in a position to let a good light fall into the throat, but the mouth should not be forced or pried open. One can nearly always gain the coöperation of children who are four or more years old (I have used this treatment on children two years old who took it satisfactorily). If one begins tactfully it is surprising to see how soon young children accept the habit of having the throat treated. It is not necessary to have the head lifted from the pillow. In order to accustom the patient to open the mouth properly I sometimes go through the manipulations of treatment once or twice with water instead of the remedy. It is very important to have the part which is to be treated well lighted, so that one may *see exactly* what is *required* and also what is *done*. If the physician does not apply the treatment himself, he should see it done whenever he can. At night a very small kerosene lamp with a reflector

which also shades the eyes of the physician, a necessary condition to success, is good. I sometimes use a small electric-light with a portable battery. It is not easy to apply local treatment properly in the throat, and the best results can only be obtained when great care is taken.

In looking over what I have written it seems to me necessary to add some details essential to success in carrying out the treatment with *strong* hydrogen-dioxide acid solutions, as there seems to be so much misconception about them as well as about the ordinary 10-volume solutions. Neutral solutions do not keep well, and alkaline ones decompose readily. The hydrogen-dioxide solutions which are sold in the market all contain some acid which increases their germicidal value and assists in preserving them.

The strong solutions of hydrogen dioxide may be made by evaporating the 10-volume solution (U.S. Pharmacopœia, 1890) in a porcelain dish over a stove or Bunsen burner; in this way one may, if one desires it, obtain a liquid containing 90 odd per cent. of hydrogen dioxide. A 50-volume solution (about 16%) of hydrogen dioxide may be readily obtained by evaporating a good 10-volume solution to $\frac{1}{6}$ of its weight; a 25-volume solution, by evaporating a good 10-volume solution to $\frac{1}{3}$ of its weight.[1]

[1] If there were no loss of hydrogen dioxide during evaporation, this process would yield a 60-volume solution, but about 20 per cent. of the dioxide is lost; therefore, in making a 50-volume solution it is necessary to evaporate a 10-volume to one-sixth instead of one-fifth of its weight. In making solutions of greater strength, the loss would be rather more; in making those of weaker strength, say 25 volumes, the loss would be less than 20 per cent. There is no economy in buying a solution that has not been well made, as it does not keep well and loses more on evaporation than a good one. The time required to evaporate over a gas stove 190 grammes of a 10-volume solution (U.S. Pharmacopœia, 1890), to 32 grammes (an ounce), of 50-volume solution, is half an hour. One may carry on the evaporation at a gentle boil at the rate of about 6 grammes (one drachm and one-half) per minute.

For commercial purposes the strong solution can doubtless be made with a smaller amount of loss. I simply suggest how in the emergency of diphtheria one may quickly obtain a strong solution. Usually I make some ounces at one time.

In the solution of the Oakland Chemical Company the free acid seems to be chiefly hydrochloric, and this is the acid which I now prefer. It is a better germicide than sulphuric acid, although not so good as nitric. Hydrogen-dioxide solutions keep better in cool than in warm places; they decompose more rapidly in sunlight.

I have lately made twenty-six experiments, extending over periods of from four to twenty-six weeks, upon the keeping qualities of hydrogen-dioxide solutions of strengths varying from 10 to over 100 volumes, and these tests show that the strong, 25 and 50 volumes, hydrogen-dioxide solutions of good make are sufficiently stable to be perfectly practicable.

Hydrogen dioxide is a bleaching agent and should not be brought into contact with

In making the strong solutions it is not necessary to add any acid, as but little of that present in the solution is lost, and 10-volume solutions containing 0.030% of acid when evaporated to $\frac{1}{6}$ of their weight contain about 0.18% of acid, and this is as much as is required for use in diphtheria.

Let me remind you in passing that the gastric juice contains 0.20% of hydrochloric acid. As this amount does not injure the lining membrane of the stomach, it could hardly injure the throat when applied for a short period only.

Bromide of potassium is of much service to adults during the first few nights, as they are very anxious when they find they have so severe a disease as diphtheria; children do not need it, as they go to sleep directly after treatment, or if asleep are frequently not fully awakened by treatment.

In many cases of retraction much relief follows the inhalation of steam or calomel fumigations.

There should be abundant and dry air in the patient's room and abundant and direct sunlight. Sunlight is especially advantageous in a diphtheria ward on account of its excellent germicidal properties, and every room in a hospital for such patients should have this. The simplest construction will permit these conditions to be fulfilled. The building should run north and south so that every bed may have sunshine part of the day. The utmost attention should be paid to the nourishment of the patient; if too little food is taken by the mouth it should be supplemented by feeding in other ways, as by the rectum or by means of a soft catheter and a funnel. The catheter may be inserted gently through the nose into the œsophagus and liquid food may be poured into the funnel.

Good food, absolute rest, protection from draught, or from a temperature that might give the patient a cold, are to be insisted upon. In some cases stimulation may be desirable. Strychnine, digitalis, and iron should be used when required.

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the hair or colored fabrics. One should avoid getting it on the skin, as it may, after a few minutes, whiten the skin and cause a pricking sensation. It is probable that it attacks the dead outer layer of the epidermis, and hence the white appearance; a minute portion of the solution may get into some small cavities of the skin, and the oxygen gas be there liberated, thus causing pressure on the endings of the sensitive nerves.

The mortality from diphtheria differs in different cities (in recent years it has been very much higher in Boston than in some other cities) and in different institutions, and may differ in the same institution during the same period of time. These variations, I believe, *usually* depend not so much upon the special medical treatment employed as upon the state in which patients are admitted and the conditions which surround them after admission; by this I mean the ventilation of the ward, the amount of sunlight, the care taken in regard to the cleanliness of the instruments, exposure to other diseases, etc. The milder cases recover if no harmful treatment is employed.

At the Boston City Hospital there are two buildings for the scarlet-fever patients; one belonging to the hospital which is used for acute cases of scarlet fever, and the other, a wooden building, placed at the disposal of the hospital less than a year ago, which is used for the convalescent cases of scarlet fever. Diphtheria has developed in both buildings, but in the first, the cases have usually been mild in character; in the second, the building for convalescents, they have been severe, among the most severe and fatal we have had at the hospital. The two buildings are erected on land that is only a few feet above high-water mark, but in the building that does not belong to the hospital the damp ground is not covered with cement as is the case in the other building.

I have used the strong hydrogen-dioxide acid solutions in over 100 cases, which varied in age from 2 to 68 years; some were cases of pseudo-diphtheria, and others were hopeless cases of diphtheria in which it was used to give comfort to the patient by getting out membrane from the throat, so that swallowing was made easier, or to keep down the septic odor; again, others were cases that came under treatment early in the disease.

These solutions fulfil the conditions sought: they will kill the bacilli of diphtheria in the laboratory in five seconds, and are not poisonous (they are readily decomposed into oxygen and water); they prevent the septic odor, and take off certain portions of the false membrane better than anything else I have employed; under their use the congestion and glandular tenderness and enlargement is

more quickly diminished, and the bacilli remain for a shorter time in the throat. Not only is the course of the disease shortened, but also the convalescence is conspicuously rapid compared with the cases under my care before I used this treatment. The patient is thus for a shorter time a menace to those around him, and the danger of the spread of the disease is much lessened. There is conspicuously less tendency to cardiac weakness.

In studying the effect of any local treatment upon the mortality it seems to me that we should consider chiefly the cases in which the treatment has not been delayed too long, say not beyond three days.

I will, therefore, discuss here two series of cases of membranous throats, occurring in different years, that were treated with strong hydrogen-dioxide solutions and comply with this condition. There were 18 in the first series, and 30 in the second series; 48 in all. During the first period there were, in all, 23 cases of membranous throats, the diagnosis of which was not based on cultures, that entered the hospital within the first three days of the disease, so far as known. Five of these do not concern us, as they were not treated with strong solutions of hydrogen dioxide, but being operative cases, were transferred directly from the medical to the surgical side of the hospital, were there intubed, and died two days after entrance. The remaining 18 make up the first series of cases treated with strong hydrogen-dioxide acid solutions within the first three days of the disease. One of these 18 cases died; this was a laryngeal case at entrance.

During the second period there were, in all, 40 cases of diphtheria, the diagnosis of which was based on cultures, that came under my care within the first three days of the disease so far as known. Ten of these cases do not concern us, for the following reasons: Seven were mild or very mild cases that recovered and were not treated with strong hydrogen-dioxide acid solutions. The eighth was a child who entered the hospital on the *second* day of the disease, but on account of extreme homesickness did not have any treatment until the *fourth* day of the disease. She was then treated with the strong hydrogen-dioxide acid solutions and recovered. The

ninth and tenth cases were not treated with the strong hydrogen-dioxide solutions until after three days, as there was none in the ward at the time, or it was deficient in strength. These two cases died. The remaining 30 cases of diphtheria, making up the second series of cases under discussion, were treated with strong hydrogen-dioxide acid solutions within the first three days of the disease, so far as known. Four-fifths of these 30 cases entered the hospital during the months in which the mortality from diphtheria in Massachusetts is greatest. Of these thirty cases two died. One was a woman, 24 years of age, who was vaccinated a few days before the attack of diphtheria began, and the solution used in this case was found to have been much below 50 volumes in strength. (In private practice I always test the solutions before using them.) The patient some years before had lost a brother and sister with diphtheria. The other was a child four years of age, who took the treatment well for one day, but became delirious the next day, so that further treatment was impracticable, and died the following day.

It gives me pleasure to testify here to the careful manner in which the house officers and nurses carried out my instructions in regard to these patients.

I have used the strong hydrogen-dioxide acid solutions at the Boston City Hospital during the years 1892, '93, and January, '94, six months in all, as well as in private practice, and have used them with increasing satisfaction.

In closing this paper I wish to emphasize the importance of the early diagnosis of diphtheria, and, if the treatment be local, of prompt, gentle, and thorough treatment during the early days of the disease with strong hydrogen-dioxide solutions of known strength, containing a proper amount of acid, applied with efficient instruments.

APPENDIX.

Since this paper was written I have used anti-toxin in a few cases ("Boston Medical and Surgical Journal," December 20, 1894) with excellent results, and initiated its use at the Boston City Hospital, where its administration in this community was begun. Under this treatment the bacilli often disappear from the throat early. In three of the cases an eruption appeared several days after the anti-toxin was injected; in three there was pain in the bones; one of these had periostitis of the ulnar and an extremely painful tenosynovitis about the left hand and wrist; two had swelling of the joints.

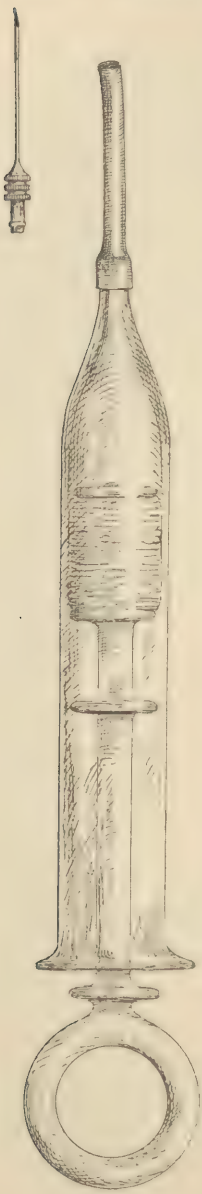

FIG. 2.

The syringe which I have designed and use to inject the anti-toxin (see Fig. 2) is a modification of the one I published in 1892; it is made of glass and packed with asbestos, and is joined to the hypodermic needle by a short piece of rubber tubing. By this device the anti-toxin is injected with greater ease into a struggling child, and the danger of breaking off the needle under the skin — an accident which may happen when the needle is rigidly fixed to the syringe — is avoided. This instrument may be sterilized by boiling in water.[1]

In Europe, local treatment is recommended to be used with anti-toxin. In some of my patients I have used anti-toxin alone, and in others I have combined with it local treatment with a 25-volume acid solution of hydrogen dioxide in the throat (made from the U.S. Pharmacopœia 10-volume solution); and in nasal diphtheria I have used in the nose a dilute (2-volume) solution. These solutions may

[1] To fill the syringe remove the needle, insert the rubber tube into the bottle of

be used every three hours in spray. The loosening and softening action of the anti-toxin, together with the disintegrating action of the hydrogen-dioxide solution, remove the membrane rapidly, and the hydrogen-dioxide solution lessens, if it does not obviate, the danger of pieces of false membrane getting into the trachea from the pharynx.

In treating diphtheria I now usually inject anti-toxin, and apply a spray of a 25-volume acid solution of hydrogen dioxide locally in the throat, and a 2-volume solution in the nose once in three or four hours.

serum and draw in the required amount; then hold the syringe vertically, with the rubber tube up, draw in air enough to fill the conical end of the syringe and put in the needle; next hold the syringe horizontally and fill the needle with serum. Insert the needle well under the skin, and inject the serum, holding the handle up; the bubble of air near the piston allows all the serum in the syringe to be injected. This syringe is made by Codman & Shurtleff, Boston, and is inexpensive.